DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)

Attorney Docket No.: 2056.001
Inventor Name: David Young et al
COMPLETE IF KNOWN
Application No: /
Filing Date:
Group Art Unit:
Examiner Name:

__X__ Decl. Sub. w/Initial Filing

___ Decl. Sub. after Initial Filing (surcharge (37 CFR 1.15 (e))

As a below named inventor, I hereby declare that:

My residence, post office addr., and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

INDIVIDUALIZED ANTI-CANCER ANTIBODIES

the specification which
__X__ is attached hereto OR
____ was filed on _____ As United States Application No. or PCT Intl. Appln. No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN NUMBERS:	COUNTRY:	FOREIGN FILING DATE:	PRIORITY NOT CLAIMED:	CERTIFIED COPY Yes	No
			____	____	____
			____	____	____
			____	____	____

__ Additional foreign appln. nos. are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below:

APPLICATION NUMBER(s): FILING DATE:

____ Addnl. provisional appln. Nos. are listed on a Supplementary priority data Sheet PTO/SB/02B attached.

DECLARATION - UTILITY or DESIGN PATENT APPLICATION

I hereby claim the benefit under 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

U.S. PARENT APPLICATION or PCT NUMBER:	PARENT FILING DATE:	PARENT PATENT NO: (if applicable)

__ Additional U.S. or PCT international appln.nos. are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: X Customer No: 21917 PLACE CUSTOMER No. BAR CODE LABEL HERE

OR

Registered practitioner(s) name/registration no. listed below.

NAME:	REGISTRATION NO:	NAME:	REGISTRATION NO:
Michael A. Slavin	34,016	Erik C. Swanson	40,194
Ferris H. Lander	43,377		

DIRECT ALL CORRESPONDENCE TO: ___ Customer Number Or Bar Code Label OR Correspondence address below

NAME:	McHale & Slavin, P.A.		
ADDRESS:	4440 PGA Blvd.,		
ADDRESS:	Suite 402		
CITY:	Palm Beach Gardens	STATE: FL	ZIP: 33410
COUNTRY:	U.S.	TELEPHONE: (561) 625-6575	FAX: (561) 625-6572

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 17 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

NAME OF SOLE OR FIRST INVENTOR: ___ A Petition has been filed for this unsigned inv.

GIVEN NAME (first and middle [if any]):	FAMILY NAME OR SURNAME:
David S. F.	Young

Inventor's signature: David S. F. Young Date: Oct 1, 1999

Residence: 51 Baldwin Street, Apt. 3

City: Toronto Ontario Country: Canada Zip: M5T 1L1 Citizenship: Canadian

Post Office Address: 51 Baldwin Street, Apt. 3, Toronto, Ontario, Canada M5T 1L1

Additional inventors are being named on the X Supplemental additional inventor(s) sheet(s) PTO/SB/02A attached hereto.

NAME OF SECOND INVENTOR: ____ A Petition has been filed for this unsigned inv.

GIVEN NAME (first and middle [if any]):	FAMILY NAME OR SURNAME:
Miyoko	Takahashi

Inventor's signature: M. Takahashi, 1st October, 1999

Residence: 65 Franklin Avenue,

City: Toronto Ontario Country: Canada Zip: M2M 1B8 Citizenship: Canadian

Post Office Address: 65 Franklin Avenue, Toronto, Ontario, Canada M2M 1B8

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Young *et al.*
Serial No.	:	09/727,361
Filed	:	November 29, 2000
For	:	**Individualized Anti-Cancer Antibodies**
Examiner	:	Susan Ungar
Art Unit	:	1642
Our File No.	:	2056.009

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

DECLARATION UNDER 37 CFR § 1.132

I, David S.F. Young, do hereby declare as follows:

1. I am the first inventor and applicant of the invention entitled "**Individualized Anti-Cancer Antibodies**", disclosed and claimed in U.S. Application Serial No. 09/727,361, filed November 29, 2000.

2. I have reviewed the Examiner's Office Action dated October 21, 2002.

3. For the purpose of evidencing the binding characteristics of the claimed antigen binding moiety (antibody or antigen binding fragment thereof) to a plurality of species of cancerous cells, the following experiments were conducted, thereby clarifying any question of enablement for claims to a process for isolating cancer cells.

An immunohistochemistry study was carried out on formalin-fixed, paraffin-embedded human tissues to profile expression of the ARH460-23 antigen on normal and tumor tissues.

Methods

The ARH460-23 antibody was tested under numerous conditions to determine reactivity in paraffin-embedded tissue sections. Normal mouse serum was run in parallel as a negative control. Four-micron sections were prepared from a number of different human tissues. Tissue sections were deparaffinized in xylenes. Steam heat induced epitope recovery (SHIER) was used with several different SHIER solutions with and without enzyme digestion tissue in two different concentrations: 20' SHIER#1, No Enzyme; 20' SHIER#1, Prot K Enzyme 1:40; 20' SHIER#2, No Enzyme; 20'SHIER#2, Prot K Enzyme 1:40; No SHIER, No Enzyme; No SHIER, Prot K Enzyme 1:15; RC-1, No Enzyme; RC-2, No Enzyme. Multiple primary antibody (ARH460-23) concentrations were used to select for the optimal concentration: 5.0mg/ml (25 min incubation); 4.0mg/ml (25 min incubation); 3.0mg/ml (25 min incubation); 2.5mg/ml (25 min incubation); 2.0mg/ml (25 min incubation). Positive controls were run to assure the detection chemistries and antigen pretreatments were working appropriately. Normal Mouse Serum was run as a negative control. This above procedure was completely automated using the TechMate 1000 or TechMate 500

(BioTek Solutions/Ventana Medical Systems). Results were obtained from 20 minute SHIER / no enzyme tissue pretreatment, overnight H460-23 incubation at 3.0mg/ml.

Slides were examined under a microscope after each run to assess staining and determine refining studies. Positive staining was indicated by a dark brown color of the chromogen (DAB-HRP enzymatic reaction product). Hematoxylin counterstain provided a blue nuclear stain to assess cell and tissue morphology. See attached Figures 1-9. Digital images of representative staining were captured using a video camera from Olympus. Images were saved as compressed jpegs and imported into a Microsoft Word document. Scoring of the specific antibody reactivity was done on the standard pathology scale of 0 to 4 where 0 is no reactivity and 4 is high reactivity. Whenever possible the tissue was scored on a subcellular level to indicate reactivity within the nucleus, cytoplasm and plasma membrane and if possible reactive cell types.

Results and Conclusions

Most tumor tissues tested were strongly positive for ARH460-23. In the colon and prostate all tumors were highly reactive and found to have both membranous and cytoplasmic binding. The one ovarian carcinoma tested yielded a similar result.

Lung and breast carcinomas and melanomas yielded more mixed results. In the lung, both large cell carcinomas were highly reactive on the cell membrane and in the cytoplasm. Of the 2 adenocarcinomas examined, one was positive for ARH460-23 binding and one negative. In breast, 7 of 9 carcinomas were positive. In medulary carcinomas where lymphocytes were present, the lymphocytes were also positive for ARH460-23 expression. Two of the 4 melanomas tested were positive and reactive in both the cell membrane and cytoplasm. In normal breast, skin, lung and ovary epithelia, ARH460-23 was either positive or weakly positive but confined to the cytoplasm and perinuclear regions of the cell. In both colon and ovary the normal tissues tested were negative for ARH460-23. However, normal colon displayed inflammatory cell reactivity in the stroma that was both membranous and cytoplasmic. When normal tissues were positive it was mainly confined to the cytoplasm and perinuclear membranes. Typically when a tumor was positive for ARH460-23 it was found to be both reactive in the membrane and cytoplasm (16 of 18 or 89%). In addition, inflammatory cells found in proximity to tumor were reactive to ARH460-23 on the cell membrane and in the cytoplasm. ARH460-23 shows reactivity in both normal and neoplastic cells as well as populations of inflammatory cells in the colon and in proximity to tumors. The antibody tends to be reactive to cell membranes in many tumors and in lymphocytes but in normal

epithelia it is mainly confined to cytoplasm and perinuclear regions.

Summary Table

Tissue Type	Tissue Pathology	Reactivity	Sample No.	Cellular Stain Localization
COLON	NORMAL adjacent or epithelial glands	NEGATIVE	3	
	CARCINOMA	POSITIVE	2	Membranous, perinuclear and cytoplasm
PROSTATE	NORMAL	POSITIVE	1	Cytoplasm
	CARCINOMA	POSITIVE	3	Membranous, perinuclear and cytoplasm
LUNG	NORMAL	POSITIVE	1	Cytoplasm and perinuclear
	ADENOCARCINOMA	NEGATIVE	1	
	ADENOCARCINOMA	POSITIVE	3	Membranous and cytoplasm
OVARY	NORMAL	NEGATIVE	1	
	CARCINOMA	POSITIVE	1	Membranous and cytoplasm
SKIN	NORMAL	POSITIVE	1	Cytoplasm and perinuclear
	MELANOMA - Metastasis to breast	POSITIVE	1	Cytoplasm
	NODULAR MELANOMA	POSITIVE	1	Membranous and cytoplasm
	MELANOMA	NEGATIVE	2	
BREAST	NORMAL	WEAK	2	Cytoplasm
	DUCTAL INVASIVE CARCINOMA moderate to poorly differentiated	WEAK	1	Membranous and cytoplasm
	DUCTAL INVASIVE CARCINOMA well to moderately differentiated	NEGATIVE	3	
	DUCTAL INVASIVE CARCINOMA well to moderately differentiated	POSITIVE	2	Membranous and cytoplasm
	DUCTAL INVASIVE CARCINOMA poorly differentiated	POSITIVE	1	Cytoplasm and perinuclear
	MEDULARY CARCINOMA well differentiated	POSITIVE	2	Membranous and cytoplasm
	HYPERPLASIA	POSITIVE	1	Cytoplasm
CONTROL PELLETS	NCIH460 Cells	POSITIVE	1	Membranous and cytoplasm
	Jurkat Cells	NEGATIVE	1	

The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the Application or any patent issuing thereon.

(DATE) Feb 18, '03

David S.F. Young

\\Ws2\staff data files\Ferris Lander's Files\FL\AMENDMNT.PAT\2056_009.132.wpd